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A nested case control study of lung cancer among New York talc workers

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Summary: This nested case control study assessed the relationship of lung cancer and time exposed to talc, while controlling for smoking, other talc exposures, and nontalc exposures. There were 22 lung cancer cases (91% smokers and 9% former smokers) and 66 controls (27% nonsmokers, 9% former smokers, and 44% smokers). Smokers were at sixfold increased risk compared to nonsmokers and ex-smokers. When stratified by smoking status, risk of lung cancer decreased with talc tenure and remained negative when excluding cases with < 20 years' latency and short-term workers. These data suggest that nontalc exposures are not confounding risk factors while smoking is, and that temporal and exposure-response relationships are consistent with a smoking etiology but not an occupational etiology for lung cancer.

Key words: Talc – Lung Cancer – Amphiboles – Case control study – Tremolite

Introduction

In 1980 the National Institute for Occupational Safety and Health (NIOSH) published a morbidity, mortality, and environmental study of miners and millers at the Gouverneur Talc Company (GTC) (Dement et al. 1980). Ten years later an updated portion of the earlier report was published as a health hazard evaluation (HHE) (Brown et al. 1990). During this period there were two other mortality studies of basically this same cohort (Stille and Tabershaw 1982; Lamm et al. 1988) as well as considerable discussion regarding the mineralogical composition of the talc and the cause of the excess lung cancer mortality. Various causes for the excess were suggested including the amphibole minerals in the talc, prior employment in other industries and/or in other New York talc companies, and smoking (Brown et al. 1983; Tabershaw and Thompson 1983; Dement and Brown 1982; Thompson 1984; Taylor 1981; Campbell et al. 1979; Campbell 1978; Kelse and Thompson 1989, 1990; Dement 1990; Virta 1985; Reger and Morgan 1990).

The original design of the HHE included updating the original cohort and conducting a nested case control study (Gamble and Piacitelli 1988). The nested case control study reported here investigates the confounding potential of non-GTC risk factors and exposure-response relationships while controlling for these risk factors and using tenure as the surrogate for exposure. Analysis by cumulative exposure remains to be published.

Materials and methods

All cases and controls were from the cohort of 710 white males of GTC talc workers employed between 1947 and 1978 with follow-up through 1983 (Gamble and Piacitelli 1988; Brown et al. 1990). All persons with lung cancer (ICD 162–163, 8th Revision) certified as the underlying cause of death on the death certificate were defined as cases. Each case was matched with three controls in whom all categories of nonneoplastic respiratory disease (ICD 460–519) and accidents (ICD E800–E949) had been excluded; controls were selected from survivors and deceased by reference to the closest match with respect to date of birth and date of hire. Controls must have survived the case, and control history ended at date of death of the case.

Information on each case and control concerning tobacco use and work history was obtained from interviews of the person himself (if living) or from relatives or friends. Interviews were conducted over the phone whenever possible, or by mail if not. Also, verification from other sources was done whenever possible. For example, several relatives were asked about smoking and work history. Information from GTC personnel records provided some pre-GTC employment history. Confirmation of previous employment was obtained when possible by contacting the previous employer directly.

Talc mining has gone on in this region of New York for many years, and some of the cases and controls had worked at other talc mines in addition to the GTC talc mine and mill. One analysis therefore adds non-GTC talc employment to that of years worked at the GTC talc mine or mill.

To control for possible confounding due to nontalc exposure, a panel of nine epidemiologists and industrial hygienists rated the risk of lung cancer associated with nontalc jobs as listed in the work histories without knowledge of case and control status. Each nontalc job was rated as "probable," "possible," or "no" risk of job-associated lung cancer; each category was given a score of 3, 1,

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and 0 respectively. A composite score for each job was compiled from the nine ratings. An individual's total score was the composite score for each job multiplied by years in that job, and summed aver all jobs. Total scores were divided into four categories of roughly comparable size. Estimates of the *odds* ratios (OR) for each category and trend analysis were used *to* assess whether non-talc exposure represented a risk factor deserving control in the exposure-response analysis.

The cases and controls were divided into two tenure groups (< 5, 5–15, 15–36; < 1, 1–9, 10–19, 20–36) for the major analyses of exposure-response relationships (Gamble and Piacitelli 1988). Since the results for both tenure analysis were similar only one tenure grouping is reported here. This analysis was done using GTC tenure with all cases and controls, and then repeated including only smokers. Additional analysis by GTC tenure for smokers only was done with exclusion of all cases and controls with: < 1 year's tenure: < 20 years' latency: < 20 years' latency and < 3 months' tenure. A similar analysis was repeated using all talc tenure (GTC plus non-GTC).

A linear trend in the OR by exposure was estimated following the methods described by Rothman (1986). Using a least squares approach to a weighted regression where $b' = b_1/b_0$, the slope b' was estimated from the equation case control $OR = b_0 + b_1 x$. The slope b' describes mathematically the change in OR for each year of tenure. Using the standard error (SE) of b', a 95% confidence interval (CI) for b' was calculated.

In addition, means of exposure were compared for cases and controls using paired and independent sample *t*-tests as appropriate. All tests were performed at the 0.05 significance level. Except for the comparison of exposure levels for cases and controls, all testing and confidence interval estimation may depend on the assumption of a large sample size.

Results

Table I summarizes descriptive information on the cases and controls. All of the 22 cases were either smokers (91%) or ex-smoken *(9%)*. while of *the* controls, *42 (64%)* were smokers, 6 (9%) ex-smokers, and 18 (27%) nonsmokers. *Cases* and controls who smoked were quite comparable in age, year of hire, and age at hire. Controls were somewhat heavier smokers than cases, and controls who smoked had almost twice the tenure of *cases* who smoked. Tables 2 and 3 present more detailed information on the 22 *cases*.

Table 1. Characteristics of lung cancer cases and controls

	Cases ($n = 22$)	Controls ($n = 66$)
Mean year of first employment	1949.7	1949.5
Mean age at first employment	34.6	34.1
Mean year of birth	1915	1915
Mean years worked		
Mean (SD)	6.6 (8.6)	9.2 (11.1) ($P = 0.08$)
Range	(0.003–23.5)	(0.003–35.3)
Mean years worked, all talc	7.7 (9.2)	9.9 (12.1) ($P = 0.12$)
Ex-smokers		
No. (%)	2 (9)	6 (9)
Mean cig/day (SD)	20 (9)	48.3 (13.3)
Mean pack years (SD)	19.5 (9.2)	57.5 (35.0)
Year of hire	1953.5	1950.0
Age at hire (SD)	37.5 (9.2)	32.5 (8.7)
Year of birth	1915.5	1916.8
Years worked [mean (SD)]		
CTC	15.3 (2.3)	4.6 (9.8) ($P = 0.11$)
All talc	15.3 (2.3)	4.9 (9.6) ($P = 0.111$
Smokers		
No. (%)	20 (91)	42 (64)
Mean cig/day (SD)	25.7 (12.0)	37.4 (12.7)
Mean pack years (SD)	53 (31.9)	61.9 (34.1)
Mean age began smoking (SD)	18.0 (3.7)	16.7 (3.5)
Year of hire	1949.3	1Y49.2
Age at hire (SD)	34.3 (8.5)	32.7 (7.02)
Year of birth	1914.7	IY16.3
Years worked [mean (SD)]		
CTC	5.4 (8.1)	10.4 (11.4) ($P = 0.08$)
All talc	6.6 (8.9)	11.5 (12.8) ($P = 0.13$)
Son-smokers		
No. (%)	0 (–)	18 (27)

Table 2. Case review of lung cancer deaths among talc miners and millers

Case no.	Age at	Smoking					Talc work history			
		Status	Age started	Latency	Cig./ day	Pack years	Age at hire	GTC latency	Tenure in years	
									GTC	All talc
1	79	S	Unk	Unk	20	62	57	22	0.02	0.02
2	77	S	17	60	40	120	42	35	0.20	0.20
3	63	S	18	45	40	90	42	21	0.05	0.05
4	75	S	Unk	Unk	20	Unk	41	34	23.5	23.5
5	52	S	19	33	3	5	47	5	5.31	5.31
6	55	S	29	26	10	8	39	16	2.83	2.83
7	62	Ex	17	45	20	36	44	18	16.7	16.7
8	68	S	12	56	20	56	35	33	0.35	3.35
9	58	S	Unk	Unk	20	Unk	34	24	0.64	1.06
10	64	S	25	39	20	38	34	30	1.49	2.02
11	59	S	14	45	30	56	36	23	11.78	23.5
12	62	S	20	42	40	84	32	30	22.51	23.5
13	63	S	Unk	Unk	20	Ullk	31	32	0.003	0.003
14	53	S	Unk	Unk	20	Unk	31	22	0.15	0.15
15	65	Ex	Unk	Unk	20	Unk	31	34	20.0	20.0
16	63	S	15	48	50	120	30	33	16.67	16.67
17	54	S	19	35	20	33	30	24	2.51	959
18	39	S	14	25	20	25	27	12	2.58	2.58
19	53	S	Unk	Unk	20	Unk	26	27	0.21	0.21
20	45	S	20	25	40	50	24	21	0.15	0.15
21	49	S	17	32	20	23	25	24	17.38	17.38
22	56	S	18	38	40	76	23	33	0.16	0.16

Unk. Unknown

Three potentially confounding risk factors are of primary concern: nontalc exposure, smoking, and non-GTC talc employment. Table 4 presents ORs for all cases and controls by estimated risk from nontalc exposure. The highest and medium-low scores showed a decreased risk while the medium-high score was slightly elevated. The slope of the OR (b') was negative (-0.0008). At the midpoint of the high nontalc exposure group (score = 377), the estimated OR from the regression model OR = $1 + b'$ (exposure) was 0.70. with 95% CI of 0.25 and 1.08. Since rhere was no trend for the risk of lung cancer to increase with nontalc exposure and therefore no apparent confounding, this factor is not controiled in further analyses.

TabIe 3 presents the risk of lung cancer by smoking category and cigarettes/day. Smoking cigarettes increased the OR for lung cancer almost sixfold compared to combined nonsmokers and ex-smokers, and 1.4 times compared to ex-smokers. There was little apparent difference in the OR for lung cancer by the number of cigarettes smoked per day. Smoking is controlled in some of the subsequenr analyses by including only cases and controls who smoked.

Table 6 presents the relative odds of lung cancer by tenure group for all cases and controls. ORs were around the null value with increasing tenure. The point estimates for the slope of the OR was negative, but the upper 95% confidence limit was positive. At 25 years' tenure the estimated OR from the regression model was 0.80 (0.55, 1.06).

When only smokers were considered. ORs were Iess than 1 with increasing tenure (Table 7). The point estimate of the slope and the upper 95% CI were both negative. At 25 years' tenure the estimated Or was 0.39 (0.11, 0.67).

Tables 8–10 present data for smokers only and include oniy cases and controls with ≥ 1 year's tenure (Table 8), ≥ 20 years' latency (Table 9), and ≥ 20 years' latency and > 3 months' tenure (Table 10). The results are similar to those observed in Table 7: the ORs all decline with increasing tenure. the siopes are negative. and the upper 95% CIs are negative. except in Table 10, where the upper 95% CI is positive.

Another possible confounder is employment at non-GTC talc mines and milk. Table 11 compares the risk of total talc employment (GTC plus non-GTC) for all cases and controls. The only change was one more case in the ≥ 15 year tenure group and one less case in the < 5 year tenure group. The OR slope was positive. and at 25 years' tenure the estimated OR was 1.03 (0.73, 1.33).

Table 12 compares the risk of total ralc employment stratified by smoking. The slope and upper 95% CI are negative. At 25 years' tenure the estimated OR is 0.54 (0.21, 0.87).

Discussion

The primary reason for this nested case control study was to try and determine whether talc exposure was the

Table 3. Case review of lung cancer deaths among talc miners and millers

Case no.	GTC employment	Non-GTC employment[a]
1	Carpenter	Construction carpenter (37). lumber camp (2) iron Mine (1)
2	Painter	Painter (35). Purchasing clerk (iron. St. Joes) (16)
3	Millwright	welder (steel mill) (10). papa mill (5)
4	Miller. oiler. forklift op.	Driller (16)
5	Laborer. oiler	Mine (>9). foundry (molder) (12).construction carpenter
6	Blacksmith and welder	Road construction (5). mine blacksmith and welder (6). car mechanic (3). welder (10)
7	Miner	Dairy farmer (35)
8	Mucker. machine man	Driller (talc. coal. zinc) (18). St. Lawrence Seaway (5)
9	Muckcr and driller	St. Joe lead (2). paper co. (2). Int. Talc (1). farm (5). army (4). unknown (13)
10	Mucker and driller	Military (7). Int. Talc (1). manufacturing (?) (18). truck driver (17)
11	Trammer. electrician. driller. Eimco op.. scraper op.. mucker	Paper mill (1). hosiery mill (3). Loomis Talc (driller. foreman) (12). construction (1). TV repair (10)
12	Muckcr. Eimco op.. driller hoistman. trammer	Mucker. driller (St. Joe Lead) (2). packer (Talc) (1). farm (3). sinking shafts (1)
13	Mucker	Driller (iron) (20). dairy farm (3). carpenter (1). construction (31)
14	Mucker	Army (4). ALCOA (5). driller (6 mo). sawmill. unknown 13). const. driller (3). Farm (11)
15	Mucker. scraper op.. Eimco op.. shaft mucker. driller	Farm. feed mill (1). operator (aluminum company) (1)
16	Miner	Farm (23). zinc miner (3).hcaw equipment op. (5). zinc mill (5)
17	Muckcr. driller	Farm. mucker/driller (talc) (7).blaster (iron Mine) (19)
18	Mucker. Eimco op.	Mucker (1). ALCOA (3 mo). military (1). manufacturing bowling pins (If. unknown (1)
19	Mucker	Army (7). manufacturing (1). miner (3mo). farm. (4 mo). sawmill (I). radio repair. TV repair (5)
20	Blacksmith	Quarry (>1). ALCOA (5). driller (iron) (4mo). roofer (hot tar) (2). machinisr (5). foundry (1)
21	Laborer. miller. cal. process op.. wheeler mill. process air op.. car finer	Piper mill (9). stock clerk (7)
22	Laborer	Road crew (3 mo). St. Joa Mineral (1). iron mint (6mo). foundry (molder) (4 mo). construction (1 mo); navy (3). custodian (22)

[a] Figures within parentheses represent years of employment. unless otherwise indicated

cause of the elevated snndardized mortality ratios (SMRs) for lung cancer which were observed in the previous cohort studies (Dement et al. 1980: Stille and Tabershaw 1982: Lamm et al. 1988) and which remained after 8 more years of foilow-up (Gamble and Piacitelli 1988: Brown et al. 1990). To do this it is necessary to address the issues of possible confounding from other occupational exposure. non-GTC talc exposures. and smoking and to evaluate exposure-response. There was no apparent confounding from other exposures as rhe ORs showed no trend to increase with increasing risk scores from nontalc employment. As expected. smoking was a risk factor for lung cancer and was more prevalent among cases than controls. thereby confounding the analysis and elevating the observed risk rario in the cohort studies. The exposure-response relationship for all cases and controls was slightly negative. but not statistically significant. When controlling for smoking the trend was negative and statistically significant: that is. as tenure increased. the ORs for lung cancer decreased and the upper 95% confidence limits were negative. The finding of a decreased risk ratio with increasing tenure was not materially affected by non-GTC talc esposure and remained when cases and controls with less than 20 years' latency.

Table 4. Lung cancer risk by nontalc exposure (panel score × years worked): all cases and controls

Score (panel score × years employed)	Cases	Controls	Odds ratio
221–533	3	13	0.55
121–220	6	13	1.10
51–120	5	21	0.57
0–50	8	19	1.00
	22	66	

Slope of OR b' (SE) = −0.0008 (0.0005): $b' = b_1/b_0$: 95% CI of b' = −0.002, +0.0002: $b = 0.82$: $b_1 = -0.0007$
Estimated OR at midpoint of high exposure group (score = 377) = $1 + b'$(score) = 1 + (−0.0008) (377) = 0.70: 95% CI: 1 + (−0.002) (377) = 0.25 (lower): 1 + (+0.0002) (377) = 1.08 (upper): $\chi^2 = 0.266$ (NS).

< 1 year's tenure, and less than 20 years' latency and 3 months' tenure were excluded.

There is a potential for misclassification of nontalc exposures and smoking history. Nontalc exposures were collected from several sources including personnel records and questionnaires administered to subjects or surrogates. Assessment of risk by the panel was done blind. The incompleteness of the non-GTC work history should be similar for both cases and dead controls. If there is a recall bias it should be greater recall for the controls than cases, If present. this would tend to increase the risk away from the null.

Smoking history was obtained by questionnaire. and from several surrogates for cases and dead controls. Two studies (Kolonel 1977: Lerchen and Samet 1986) indicate 96% and 100% agreement of smoking status when comparing wives' responses to those of their husbands. Thus classification by smoking status is likely to be quire good. If there is recall bias it is most likely to be less recollection among cases than among controls.

Increased risk of lung Cancer was present among workers with short tenures (Dement et al. 1980: Brown et al. 1990: Lamm et al. 1988). Several possible explanations have been given for this observation (Brown et al. 1990). One is that exposure to other lung carcinogens may have occurred via non-GTC employment. Six of the 22 cases had some known non-GTC talc employment. No increased risk was found for either nontalc employment nor for total talc employment (both GTC and non-GTC) when controlling for smoking. Second, it has been suggested that short-term employees may have had very high exposures. In this study cases were matched on date of hire and so controls had as great an opportunity of high exposure as did cases. Further. removing short-term workers (≤ I year's tenure) from the analysis did not affect the results. Thus these hypothetical explanations do not appear to be valid.

Another purpose for conducting the case control study was to adjust for possible confounding effects of smoking. In an SMR analysis using the U.S. population as a standard, the smoking habits of the exposed and referent populations may differ. thereby in part explaining the high risk ratio for the talc workers. It has been suggesred that smoking alone does not account for the excess as the 1976 smoking habits of the GTC workers "were not much different from those of U.S. white males" (Brown et al. 1990). However. the smoking habits of the 1976 GTC workforce do not necessarily reflect the smoking habits of the cases. One way to employ a more appropriate reference group is to use workers drawn from the same population as the cases. as was done in this study. Such an internal comparison population shows quite differenr smoking patterns from the cases; 91% smokers among cases vs 64% among controls- and 0% nonsmokers among cases vs 27% among controls.

Another argument against smoking explaining the excess risk is "even if 100% of the cohort were smokers. the risk for lung cancer would have been increased only by 60% or an SMR of 160" (Brown et al. 1990). As it

Table 5. Lung cancer risk by smoking status and cigarettes smoked/day: all cases and controls [smokers compared to (1) ex-smokers and nonsmokers and (2) ex-smokers only]

	Cases	Controls	Odds ran'(95% CI)	
Smoker	20	42	5.71 (0.36. 7.81)	1.43 (0.31. 9.07)
Ex-smoker	2	6	1.0 (Ex-smoker and nonsmoker)	1.00 (Ex-smoker only)
Nonsmoker	0	18		
	22	66		
Cigarettes/day				
> 40	6	11	6.55	1.64
20–39	12	27	5.33	1.33
1–19	2	4	6.0	1.5
Ex-smokers	2	6		1.00 (ex-smoker only)
Nonsmokers	0	18	1.00 (ex-smoker and nonsmoker)	
	22	66		

Slope of OR when reference group = ex-smokers and nonsmokers: b' (SE) = −0.12 (0.008): 95% CI = 0.105, 0.14: $b_0 = 1.09$: $b_1 = 0.13$
Estimated OR for 20 cig/day smoker = 1 + (0.12)(20) = 3.42 (3.10, 3.75): $\chi^2 = 4.68$

Table 6. Lung cancer risk by tenure at GTC: all cases and Controls

Tenure-years	Caws	Controls	Odds ratio
15–36	6	21	0.82
5–15	a	5	1.14
<5	14	40	1.00
	22	66	

Slope of OR b' (SE) = −0.008 (0.003): $b' = b_1/b_0$: 95% CI of b' = −0.018. +0.002: b_0 = 1.03: b_1 = −0.008
Estimated OR (95% CI) at 25 years' tenure = 1 − (−0.008) (25) = 0.80 (0.55. 1.06): χ^2 = 0.13 (NS)

Table 7. Lung cancer risk by tenure at GTC: smokers only

Tenure-years	Cases	Controls	Odds ratio
U-36	4	15	0.42
5–15	2	5	0.63
<5	14	22	1.00
	20	42	

Slope of OR b' (SE) = −0.024 (0.006): 95% CI = −0.04. −0.01: b_0 = 1.04: b_1 = −0.03
Estimated OR (95% CI) at 25 years' tenure = 1+ (−0.02) (25) = 039 (0.11. 0.67): χ^2 = 1.78 (NS)

Table 8. Lung cancer risk by tenure at GTC: smokers only with ≥ 1 year's tenure

Tenure-yean	Cases	Controls	Odds ratio
15–36	4	15	0.53
5–15	2	5	0.80
1– 5	4	8	1.0
	10	28	

Slope of OR b' (SE) = −0.019 (0.007): 95% CI = −0.03. −0.006: b_0 = 1.04: b_1 = −0.02
Estimated OR (95% CI) at 25 years' tenure = 1 + (−0.0191 (25) = 0.52 (0.19. 0.84): χ^2 = 0.577

Table 9. Lung Cancer risk by tenure at GTC: smokers only with ≥ 20 years latency

Tenure-years	Cases	Controls	Odds ratio
15–36	4	15	0.49
S–15	I	4	0.46
<5	12	22	1.0
	17	41	

Slope of OR b' (SE) = −0.021 (0.006): 95% CI = (−0.03. −0.01): b_0 = 1.01: b_1 = −0.02
Estimated OR at 25 years' tenure = 1 − (−0.021) (25) = 0.47 (0.19. 0.75): χ^2 = 1.152

turns our. 100% of the cases were smokers. The overall SMR for lung cancer was 207. with a lower 95% CI of 120: in the ≥ 20 year latency group. the SMR was 260 with a lower 95% CI of 137. Thus one cannot distinguish between the hypothetical SMR of 160 and the actual

Table 10. Lung cancer risk by tenure at GTC: smokers only with ≥ 20 years latency and > 3 months tenure

Tenure-years	Cases	Controls	Odds ratio
15–36	4	15	0.73
5–15	I	4	0.69
3mo–5yr	4	11	1.0
	9	30	

Slope of OR b' (SE) = −0.01 (0.01): 95% CI (−0.02. +0.003): b_0 = 0.98: b_1 = −0.01
Estimated OR at 25 years' tenure = 1 + (−0.01) (25) = 0.74 (0.40. 1.08): χ^2 = 0.120

Table 11. Lung cancer risk by *total* talc tenure: all cases and controls

Tenure-years	Cases	Controls	Oddsratio
15–41	7	21	1.08
5-15	2	5	1.23
<5	13	40	1.0
	22	66	

Slope of OR b' (SE) = +0.001 (0.006): 95% CI = −0.01. +0.01: b_0 = 1.08: b_1 = 0.001
Estimated OR at 25 years' tenure = 1 + (0.001) (25)= 1.08 (0.73. 1.33): χ^2 = 0.002 (NS)

Table 12. Lung cancer risk by *total* talc tenure: smokers only

Tenure-years	Cases	Controls	Odds ratio
15–41	5	15	0.56
5–15	2	5	0.68
<5	13	22	1.0
	20	42	

Slope of OR b' (SE) = −0.02 (0.01): 95% CI: –0.03. −0.005; b_0 = 1.03: b_1 = −0.02
Estimated OR at 25 years' tenure = 1 + (−0.02) (25) = 0.54 (0.22. 0.87): χ^2 = 0.84 (NS)

SMR for either all the lung cancer cases or for those with ≥ 20 years' latency. The inverse and statistically signifi-Cant exposure-response trend found in the case control analysis points up the confounding effect of smoking in the cohort analyses. The lack of an exposure-response trend with talc tenure is contrary to conventionai wis-dom and to the conclusion that workplace talc exposures account for the increased risk of lung cancer.

Temporality is the only standard that may provide in-disputable evidence thar an association is not causal (Rothman 1986). A period of 20 or more years is a com-monly used period between first exposure and the induc-tion of lung cancer (Selikoff er al. 1980). Since death often occurs fairly shortly after diagnosis of the disease. the time between date of hire (or date of starting smok-ing) and date of death is used as the latency period.

The range of latency for asbestos workers at highest risk (textiles. insulation) and with long esposure is about 28–34 years (Selikoff et al. 1980; Knos et al. 1968: De-ment et al. 1983). For a cohort exposed to high levels of

amosite for short periods. the mean latency is lower (21 years). (Seidman et al. 1986). as it is for vermiculite and asbestos cement workers (Weill et al. 1979: Amandus and Wheeler 1987). Chrysotile miners and millers. regardless of smoking habits or asbestos *exposure*. have a mean latency of about 40 years (Liddell 1980).

For mining cohorts exposed to nonasbestiform amphiboles (and for which there are no apparent exposure-response or causative relationships). the mean latency ranges from 22 to 32 years (Brown et al. 1986: Cooper et al. 1988). Smokers have a latency of about 40 years (Liddell 1980: Wynder and Stellman 1977).

The mean time from date of hire till death in GTC cases was 25 years: the length of time since starting smoking was 40 years. Thus the criterion of temporality suggests smoking is a more plausible risk factor for lung cancer than talc.

Analysis of exposure-response is an important element in the assessment of causality in this study. Misclassification of exposure will generally reduce the risk toward the null. The use of tenure as a surrogate estimate of exposure will not result in misclassification if subjects have the same exposure over time (Johnson 1986). If exposure is nor the same over time then it may be difficult to show an exposure-response relationship or observe decreased risk with increased tenure. By matching for the period of exposure-there is some control for changes in exposure over time. To reduce the possibility of exposure misclassification. analysis of exposure-response using as *the* exposure variables net tenure (actual hours each employee worked) and cumulative quantitative estimates of dust exposure shouid be completed. The lack of such analyses does not. however. negate the observed inverse exposure-responserelationship.

Another important criterion for evaluating causality is consistency. There is evidence the talc contains nonasbestiform amphiboles and a minor talc fiber component (Campbellet al. 1979: Campbell 1978: Kelse and Thompson 1989. 1990: Virta 1985). Mineral content of the talc varies somewhat but is generally in the range of 40%–60% tremolire. 1%–10% anthophyllite. 20%–40% talc. 20%–30% serpentine (antigorite-lizardite). and 0%–2% quartz (Kelse and Thompson 1989). NIOSH in 1980 reported over 70% tremolite and anthophyllite fibers in bulk and airborne samples from the talc mine that satistied the regulatory. definition of ≥ 3:1 aspect ratio and >5 µm length (Dement et al. 1980). A mineralogical definition of asbestiform mineral fiber populations requires the presence of many particles >5 urn long with aspect ratios greater than 20:1 and thin fibrils <0.5 µm in width. Analysis of both hulk and airborne particles from the talc mine traditionally show little to no particles with an aspect ratio of 20:1 or greater, and none showed such asbestiform characteristics as splayed ends. curvature. or parallel fibers occurring in bundles for the amphibole components. For comparison. about 50% (37%–65%) of airborne fibers from asbestos mining and bagging operations had aspect ratios >20:1. About 3% (0%–6%) of airborne cleavage fragments from other nonasbestiform amphibole mines (cummingtonite. actinolite grunerite/actinolite) have aspect ratios >20:1. The width of airborne cleavage fragmer asbestos fibers is also distinctly different. About 6 amphibole asbestos and chrysotile fibers are >0. wide while 100% of amphibole and tremolite talc age fragments are >0.25 µm in width (Kelse and Th son 1989)-Based on these mineralogical characteri this cohort of talc miners is considered to be expos talc containing nonasbestiform tremolite.

Other cohort studies of workers exposed to nonas tiform amphiboles (Brown et al. 1986: Cooper e 1988) show a lack of relationship between tenure risk of lung cancer similar to that shown by the cohort. No causal relationship is postulated in these horts mining nonasbestiform amphiboles.

Asbestos-exposed cohorts do show increased risk w increasing tenure (Seidman et al. 1986: Weill et al. 19 Amandus and Wheeler 1987: McDonald JC et al. 198 McDonald AD et al. 1983a b. 1984: Hobbs et al. 198 Hughes et al. 1987: Ohlson and Hoystedt 1985) and causal relationshipis postulated. Workers exposed to as bestos were used to compare the consistency of the te nure-lung cancer association because of the contention that the talc contains asbestos [Dement et al. 1980: Demenr and Brown 1982: Dement 1990). Thus the negative slope of the exposure-response curve (using tenure as a surrogate for exposure) is opposite to the effect one would expect if talc exposure were to increase the risk of lung cancer. is consistent with exposure-response relationships observed in populations mining nonasbestiform amphiboles. and is inconsistent with results from asbestos-exposed populations.

The SMRs for lung cancer (as well as for several other causes of death) are elevated in this group of talc workers- Howerer. after adjustment for the confounding effect of smoking and the postulated role of very high exposures of short-term workers, the risk ratio for lung cancer decreases with increasing tenure. The lack of an exposure-response gradient is not consistent with a causal relationship. The time occurrence of lung cancer among these talc workers is more congruent with a smoking than a talc etiology.

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